

3

Docket No. TPI-T600XC1
Serial No. 09/994,585Amendments to the Claims:Claim 1 (withdrawn):

An array for screening to identify conditions, compounds, or compositions that inhibit, prevent, induce, modify, or reverse transitions of physical state comprising at least 24 samples, each sample comprising a medium, wherein one or more of the samples comprises a disease-causing substance.

Claims 2-14 (canceled).Claim 15 (withdrawn):

A method of preparing an array of at least 24 samples for screening to identify conditions, compounds, or compositions that inhibit, prevent, induce, modify, or reverse transitions of physical state comprising: (a) adding a medium to each of the samples; and (b) adding a disease-causing substance to at least one of the samples.

Claims 16-50 (canceled).Claim 51 (withdrawn):

A method to discover conditions, compounds, or compositions that prevent or inhibit crystallization, precipitation, polymerization, or deposition of a disease-causing substance, or promote depolymerization comprising: (a) preparing an array comprising at least 24 samples each sample comprising a medium and one or more components to induce a disease-causing substance; (b) processing one or more of the samples to induce crystallization, precipitation, or deposition of the disease-causing substance; (c) screening the array by analyzing the processed samples to detect the absence of crystallization, precipitation, polymerization, depolymerization, or deposition of the disease-causing substance; and (d) selecting the samples wherein crystallization, precipitation, polymerization, depolymerization, or deposition of the disease-causing substance did not occur to identify the conditions, compounds, or compositions.

J:\TPI\T600XC1\PTO\resp2.d.doc/DNB/ohm

Claims 52-65 (canceled).Claim 66 (withdrawn):

A method to discover conditions, compounds or compositions that promote dissolution, destruction, or breakup of a disease-causing substance, comprising: (a) preparing an array comprising at least 24 samples each sample comprising a medium and the disease-causing substance; (b) processing one or more of the samples to induce the dissolution, destruction, or breakup of the disease-causing substance; (c) screening the array by analyzing the processed samples to detect the dissolution, destruction, depolymerization, or breakup of the disease-causing substance; and (d) selecting the samples wherein the dissolution, destruction, depolymerization, or breakup of the disease-causing substance occurred to identify the conditions, compounds, or compositions.

Claims 67-80 (canceled).Claim 81 (new):

A method of screening an array of at least 96 samples to identify conditions, compounds, or compositions that inhibit or prevent transitions of physical state comprising:

(a) preparing and identifying an array of at least 96 samples in tubes and support plates or in sample well plates and dispensing a medium, a disease-causing substance in liquid or dissolved form and one or more additional components into sample tubes or sample wells with an automated distribution mechanism, and each sample differs with respect to at least one of:

the amount or concentration of the disease-causing substance;

an identity of one or more of the additional components; or

an amount or concentration of one or more of the additional components;

(b) processing one or more of the samples to induce crystallization, precipitation or deposition of the disease causing substance;

JATPMT600XC1\PTO\resp2d.doc/DNB/elun

5

Docket No. TPI-T600XC1
Serial No. 09/994,585

- (c) analyzing the processed samples to detect the induction of said crystallization, precipitation or deposition; and
- (d) selecting those processed samples that exhibit inhibition or prevention of a transition in physical state.

Rule
1-126
↓

⁸²
Claim 83 (new):

The method of claim 81, comprising dispensing said disease-causing substance in dissolved form.

⁸³
Claim 84 (new):

The method of claim 81, comprising dispensing said disease-causing substance in liquid form.

⁸⁴
Claim 85 (new):

The method of claim 81, wherein said processing comprises heating said samples in a sample incubation module to a temperature (T1), analyzing said samples for the presence of undissolved solids using visual analysis, and cooling said samples to a final temperature (T2).

⁸⁵
Claim 86 (new):

The method of claim 81, comprising the addition of said samples to tubes in a support plate.

⁸⁶
Claim 87 (new):

The method of claim ⁸⁵86, wherein said tubes are glass tubes and said support plate is a metal support plate.

⁸⁷
Claim 88 (new):

The method of claim ⁸⁵86, comprising sealing said tubes with a cap.

J:\TPI\T600XC1\PTO\resp2d.doc/DNB/clm

Rule
1-126
↓

⁸⁸
Claim 89 (new):

The method of claim ⁸⁷88, wherein said cap is pierced with a standard syringe needle and fluid aspirated through the syringe tip to remove solvent from the sample.

⁸⁹
Claim 90 (new):

The method of claim 81, wherein said array comprises at least 1000 samples.

⁹⁰
Claim 91 (new):

The method of claim 81, further comprising the generation of a work list for instructing an automated distribution mechanism to prepare said array of samples.

⁹¹
Claim 92 (new):

The method of claim 81, wherein said sample contains less than 1 milligram of said disease-causing substance.

⁹²
Claim 93 (new):

The method of claim ⁸⁷88, comprising the piercing of said cap and aspiration of medium from said samples.

⁹³
Claim 94 (new):

The method of claim 81, comprising analyzing said array of samples with a polarized light filter apparatus.

⁹⁴
Claim 95 (new):

The method of claim 81, wherein the additional component is a small molecule.

⁹⁵
Claim 96 (new):

The method of claim 81, wherein said array comprises at least 1 sub-array.

J:\TPI\T600XC1\PTO\resp2d.doc/DNB/ebm

7

Docket No. TPI-T600XC1
Serial No. 09/994,585

Rule
1-126
↓

⁹⁶
Claim 97 (new):

The method of claim 81, wherein said array comprises at least 1 sub-array with at least 24 samples.

⁹⁷
Claim 98 (new):

The method of claim 81, wherein said processing comprises adjusting a time of incubation.

⁹⁸
Claim 99 (new):

The method of claim 81, wherein said processing comprises adjusting a temperature.

⁹⁹
Claim 100 (new):

The method of claim 81, wherein said processing comprises adjusting a pressure.

¹⁰⁰
Claim 101 (new):

The method of claim 81, wherein said processing comprises subjecting the samples to a nucleation event.

¹⁰¹
Claim 102 (new):

The method of claim 81, wherein said processing comprises subjecting the samples to ultrasound, shock waves, laser energy, or mechanical stimulation.

¹⁰²
Claim 103 (new):

The method of claim 81, wherein said processing comprises adjusting an amount of a component.

¹⁰³
Claim 104 (new):

The method of claim 81, wherein said processing comprises adding a component.

J:\TPI-T600XC1\PTO\resp24.doc/DNB/ehm

8

Docket No. TPI-T600XC1
Serial No. 09/994,585

Rule
1.126
↓

Claim ¹⁰⁴105 (new):

The method of claim 81, wherein said processing comprises adjusting an amount of the medium.

Claim ¹⁰⁵106 (new):

The method of claim 81, wherein said processing comprises adjusting a gas composition.

Claim ¹⁰⁶107 (new):

The method of claim 81, wherein the disease-causing substance is calcium phosphate, calcium carbonate, calcium pyrophosphate, brushite, apatite, hydroxyapatite, calcium oxalate, a kidney stone, bone tissue, magnesium ammonium phosphate, uric acid, a salt of uric acid, a gall stone, cholesterol, an amyloid protein, collagen, bilirubin, a salt of bilirubin, dental plaque, dental calculus, protein structure, a protein precipitate, a hydrate thereof or a mixture thereof.

Claim ¹⁰⁷108 (new):

The method of claim 81, wherein the processed samples are analyzed to detect a solid or an absence of a solid.

Claim ¹⁰⁸109 (new):

The method of claim ¹⁰⁷108, wherein a detected solid is analyzed to determine if the solid is amorphous or crystalline.

Claim ¹⁰⁹110 (new):

The method of claim 81, wherein at least about 100 samples are screened per day.

Claim ¹¹⁰111 (new):

The method of claim ¹⁰⁶107, wherein at least about 1000 samples are screened per day.

JAIPAT600XC1\PTO\resp2d.doc/DNB/ahm

Rule 1.126
↓

Claim 112¹¹¹ (new):

The method of claim 81, wherein an individual sample within said array is subjected to processing methods that are different from the processing methods to which another sample is subjected.

Claim 113¹¹² (new):

The method of claim 112¹¹¹, wherein said individual sample is subjected to processing methods comprising introducing a nucleation event.

Claim 114¹¹³ (new):

The method of claim 112¹¹¹, wherein said individual sample is subjected to processing methods comprising adding one or more additional components.

Claim 115¹¹⁴ (new):

The method of claim 81, wherein said array comprises sub-arrays, and wherein an individual sample within a sub-array is subjected to processing methods that are different from the processing methods to which another sample within the sub-array is subjected.

Claim 116¹¹⁵ (new):

The method of claim 115¹¹⁴, wherein said individual sample is subjected to processing methods comprising introducing a nucleation event.

Claim 117¹¹⁶ (new):

The method of claim 115¹¹⁴, wherein said individual sample is subjected to processing methods comprising adding one or more additional components.

10

Docket No. TPI-T600XC1
Serial No. 09/994,585

Rule
1.126
↓

¹¹⁷
Claim 118 (new):

The method of claim 81, wherein said array comprises sub-arrays, and wherein an individual sub-array is subjected to processing methods that are different from the processing methods to which another sub-array is subjected.

¹¹⁸
Claim 119 (new):

The method of claim ¹¹⁷118, wherein said individual sub-array is subjected to processing methods comprising introducing a nucleation event.

¹¹⁹
Claim 120 (new):

The method of claim ¹¹⁷118, wherein said individual sub-array is subjected to processing methods comprising adding one or more additional components.

¹²⁰
Claim 121 (new):

The method of claim 81, wherein said disease-causing substance has a molecular weight less than about 1000 g/mol.

¹²¹
Claim 122 (new):

The method of claim 81, wherein the amount of said disease-causing substance in each sample is less than about 1 milligram.

¹²²
Claim 123 (new):

The method of claim 81, wherein the amount of said disease-causing substance in each sample is less than about 100 micrograms.

¹²³
Claim 124 (new):

The method of claim 81, wherein the amount of said disease-causing substance in each sample is less than about 100 nanograms.

J:\TPI\T600XC1\PTO\resp2d.doc/DNB/ebm

11

Docket No. TPI-T600XC1
Serial No. 09/994,585

Rule
1.126
↓

¹²⁴
Claim 125 (new):

The method of claim 81, wherein each sample has a total volume between 5-500 μ l.

¹²⁵
Claim 126 (new):

The method of claim 81, wherein each sample has a total volume between 10-200 μ l.

¹²⁶
Claim 127 (new):

The method of claim 81, wherein one or more samples differ from one or more other samples with respect to the amount of the disease-causing substance.

¹²⁷
Claim 128 (new):

The method of claim 81, wherein one or more samples differ from one or more other samples with respect to the amount of the medium.

¹²⁸
Claim 129 (new):

The method of claim 81, wherein one or more samples differ from one or more other samples with respect to the amount of the identity or the amount of the components.

¹²⁹
Claim 130 (new):

The method of claim 81, wherein crystal nucleation and growth is controlled by the concentration of components.

¹³⁰
Claim 131 (new):

The method of claim 81, wherein crystal nucleation and growth is controlled by the identities of components.

¹³¹
Claim 132 (new):

The method of claim 81, wherein crystal nucleation and growth is controlled by temperature.

J:\TPI\T600XC1\PTO\resp24.doc/DNB/clm

12

Docket No. TPI-T600XC1
Serial No. 09/994,585

Rule
1.126
↓

¹³²
Claim 133 (new):

The method of claim 81, wherein said analyzing is by machine vision technology.

¹³³
Claim 134 (new):

The method of claim 81, wherein said analyzing is by video-optical microscopy.

¹³⁴
Claim 135 (new):

The method of claim 81, wherein said analyzing is by image analysis.

¹³⁵
Claim 136 (new):

The method of claim 81, wherein said analyzing is by polarized light analysis.

¹³⁶
Claim 137 (new):

The method of claim 81, wherein said analyzing is by near field scanning optical microscopy.

¹³⁷
Claim 138 (new):

The method of claim 81, wherein said analyzing is by far field scanning optical microscopy.

¹³⁸
Claim 139 (new):

The method of claim 81, wherein said analyzing is by atomic-force microscopy.

¹³⁹
Claim 140 (new):

The method of claim 81, wherein said analyzing is by micro-thermal analysis.

¹⁴⁰
Claim 141 (new):

The method of claim 81, wherein said analyzing is by infrared spectroscopy.

J:\TPI\T600XC1\PTO\resp24.doc/DNB/ehm

13

Docket No. TPI-T600XC1
Serial No. 09/994,585

Rule
1.126
↓

¹⁴¹
Claim 142 (new):

The method of claim 81, wherein said analyzing is by near infrared spectroscopy.

¹⁴²
Claim 143 (new):

The method of claim 81, wherein said analyzing is by Raman spectroscopy.

¹⁴³
Claim 144 (new):

The method of claim 81, wherein said analyzing is by NMR.

¹⁴⁴
Claim 145 (new):

The method of claim 81, wherein said analyzing is by x-ray diffraction.

¹⁴⁵
Claim 146 (new):

The method of claim 81, wherein said analyzing is by neutron diffraction.

¹⁴⁶
Claim 147 (new):

The method of claim 81, wherein said analyzing is by powder x-ray diffraction.

¹⁴⁷
Claim 148 (new):

The method of claim 81, wherein said analyzing is by light microscopy.

¹⁴⁸
Claim 149 (new):

The method of claim 81, wherein said analyzing is by second harmonic generation.

¹⁴⁹
Claim 150 (new):

The method of claim 81, wherein said analyzing is by electron microscopy.

¹⁵⁰
Claim 151 (new):

The method of claim 81, wherein said analyzing is by an *in vitro* assay.

J:\TPI\T600XC1\PTO\resp2\1.doc/DNB/cha